



Applicants: Philip O. Livingston and Friedhelm Helling
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Add the following new claims 100-126.

--100. (New) A composition which comprises:

- a) a conjugate comprising (i) a GM2 or a GD2 ganglioside derivative, which derivative comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) a derivative of Keyhole Limpet Hemocyanin;
- b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and
- c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2 and GD2, whichever is present as a derivative in the conjugate,

wherein in the conjugate the ganglioside derivative is covalently bound to the derivative of Keyhole Limpet Hemocyanin through a C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative to an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin, wherein the C-4 carbon is present in a CH₂ group.

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--101. (New) The composition of claim 100, wherein the saponin is QS-21. --

--102. (New) The composition of claim 100, wherein the amount of the conjugate is an amount of between about 1

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µg and about 200 µg. --

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--103. (New) The composition of claim 102, wherein the amount of the conjugate is an amount of between 10 µg and 90 µg. --

--104. (New) The composition of claim 102, wherein the amount of the conjugate is an amount of between 10 µg and 70 µg. --

--105. (New) The composition of claim 102, wherein the amount of the conjugate is an amount of between 10 µg and 50 µg. --

--106. (New) The composition of claim 102, wherein the ganglioside derivative is a GM2 ganglioside derivative and wherein the amount of the conjugate is an amount of about 30 µg. --

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--107. (New) The composition of claim 102, wherein the ganglioside derivative is a GD2 ganglioside derivative and wherein the amount of the conjugate is an amount of about 70 µg. --

--108. (New) The composition of claim 100, wherein the amount of the saponin is an amount of between about 10 µg and about 200 µg. --

--109. (New) The composition of claim 108, wherein the amount of the saponin is about 100 µg. --

--110. (New) The composition of claim 108, wherein the amount of the saponin is about 200 µg. --

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--111. (New) The composition of claim 100, wherein the GM2 or GD2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1. --

--112. (New) A composition which comprises:

a) a conjugate comprising (i) a GM2 or a GD2 ganglioside derivative, which derivative comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) a derivative of Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree, wherein the saponin is QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the conjugate is present in an amount between about 10 µg and about 50 µg, the amount of the saponin is about 100 µg and the GM2 or GD2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, where the amount of such conjugate and such saponin is effective to stimulate or enhance production in a subject of an antibody to GM2 and GD2, whichever is present as a derivative in the conjugate;

and wherein in the conjugate the ganglioside derivative is covalently bound to the derivative of Keyhole Limpet Hemocyanin through a C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative to an ε-aminolysyl group of Keyhole Limpet Hemocyanin, wherein the C-4 carbon is present in a CH₂ group.

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--113. (New) A method of treating a subject afflicted with melanoma which comprises administering to said subject an amount of the composition of claim 112 effective to stimulate or enhance production of an antibody directed to at least one of GM2 and GD2 and to thereby treat said melanoma in said subject. --

--114. (New) A method of stimulating or enhancing production of an antibody directed to GM2 or GD2 in a subject which comprises administering to the subject an effective amount of a composition which comprises:

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a) a conjugate comprising (i) a GM2 or a GD2 ganglioside derivative, which derivative comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) a derivative of Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2 and GD2, whichever is present as a derivative in the conjugate,

wherein in the conjugate the ganglioside derivative is covalently bound to the derivative of Keyhole Limpet Hemocyanin through a C-4 carbon of the altered sphingosine

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base of the altered ceramide portion of the ganglioside derivative to an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin, wherein the C-4 carbon is present in a CH₂ group, so as to thereby stimulate or enhance production of the antibody to GM2 and GD2 in the subject, whichever is present as a derivative in the conjugate. --

--115. (New) A method of treating a cancer in a subject which comprises administering to the subject an effective cancer-treating amount of a composition which comprises:

a) a conjugate of (i) a GM2 or a GD2 ganglioside derivative, which derivative comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) a derivative of Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2 and GD2, whichever is present as a derivative in the conjugate;

wherein in the conjugate the ganglioside derivative is covalently bound to the derivative of Keyhole Limpet Hemocyanin through a C-4 carbon of the sphingosine base of the ceramide portion of the ganglioside derivative to an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin, and wherein the C-4 carbon is present in a CH₂ group, so as to thereby

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stimulate or enhance production of the antibody to GM2 and GD2 in the subject, whichever is present as a derivative in the conjugate. --

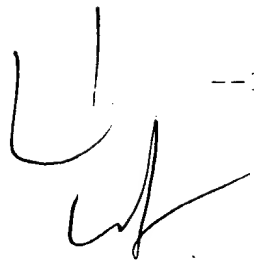
--116. (New) The method of claim 115, wherein the cancer is of epithelial origin. --

--117. (New) The method of claim 115, wherein the cancer is of neuroectodermal origin. --

--118. (New) The method of claim 117, wherein the cancer of neuroectodermal origin is a melanoma. --

--119. (New) The method of claim 114 or 115 wherein the administering is effected at two or more sites. --

--120. (New) The method of claim 119, wherein the administering is effected at three sites. --



--121. (New) The method of claim 114 or 115, wherein the composition is administered subcutaneously to said subject.--

--122. (New) The method of claim 121, wherein the composition is administered to said subject at two-week intervals.--

--123. (New) The method of claim 121, wherein the composition is initially administered to said subject at weekly intervals.--

--124. (New) The method of claim 114 or 115, wherein the composition to be administered is prepared prior to

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administration to the subject by mixing the conjugate and the saponin.--

--125. (New) The method of claim 124, wherein the conjugate and the saponin are mixed on the day of administration to the subject.--

--126. (New) A method of delaying recurrence of melanoma in subjects at risk of relapse of melanoma which comprises administering to the subject an effective melanoma treating amount of a composition which comprises:

a) a conjugate comprising (i) a GM2 or a GD2 ganglioside derivative, which derivative comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) a derivative of Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2 and GD2, whichever is present as a derivative in the conjugate,

wherein in the conjugate the ganglioside derivative is covalently bound to the derivative of Keyhole Limpet Hemocyanin through a C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside